STIC

Lucas, Z
10/630590

(FILE 'CAPLUS' ENTERED AT 10:55:01 ON 03 JAN 2005)
L1 1364 SEA FILE=CAPLUS ABB=ON PLU=ON (HUMAN(W)PAPILLOM? OR HPV)(3W)" E6" OR HUMAN WART VIRUS
L2 25 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND (PDZ? OR MAGI(2W)(I OR 1))
L3 25 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (PROTEIN OR PEPTIDE OR POLYPEPTIDE OR POLYPROTEIN)
L4 3 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND ANTIBOD?

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Nov 2004
ACCESSION NUMBER: 2004:999612 CAPLUS
DOCUMENT NUMBER: 141:420421
TITLE: Drug screening method for cancer associated with human papillomavirus infections
INVENTOR(S): Lu, Peter S.; Bagowski, Christoph Peter; Schweizer, Johannes; Diaz-Sarmiento, Chamorro Somoza; Garman, Jonathan David; Belmares, Michael P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 191 pp., Cont.-in-part of U.S. Ser. No. 630,590.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229298	A1	20041118	US 2004-789102	20040227
US 2003049695	A1	20030313	US 2002-80273	20020219
WO 2003014303	A2	20030220	WO 2002-US24655	20020802
WO 2003014303	A3	20030814		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004018487	A1	20040129	US 2003-630590	20030729

PRIORITY APPLN. INFO.:

US 2000-710059	B2	20001111
US 2001-269523P	P	20010216
US 2001-309841P	P	20010803
US 2002-80273	A2	20020219
US 2002-360061P	P	20020225
WO 2002-US24655	A2	20020802
US 2003-450464P	P	20030227
US 2003-490094P	P	20030725
US 2003-630590	A2	20030729
US 2001-269522P	P	20010216
US 2001-269694P	P	20010216
US 2002-409298P	P	20020909

Searcher : Shears 571-272-2528

AB The invention provides methods and compns. for treating pathogen infections, particularly human papillomavirus infections. Specifically, the invention provides a method of screening that involves determining an effect of a candidate agent on binding of an E6 **protein** from an oncogenic strain of HPV to a **polypeptide** containing the amino acid sequence of a particular **PDZ** domain from the cellular **protein MAGI-1**. The invention provides methods to treat diseases associated with expression of pathogen **proteins** by modulating their interactions with **MAGI-1**, and a number of isolated **peptides** useful in such methods. Also provided are kits for performing the subject methods.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Mar 2004
ACCESSION NUMBER: 2004:220171 CAPLUS
DOCUMENT NUMBER: 140:269020
TITLE: Methods of diagnosing cervical cancer by detecting oncogenic **human papillomavirus E6 proteins** using **E6**-binding partners, such as **PDZ** domain **proteins**
INVENTOR(S): Lu, Peter S.; Schweizer, Johannes; Diaz-Sarmiento, Chamorro Somoza; Belmares, Michael P.
PATENT ASSIGNEE(S): Arbor Vita Corporation, USA
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004022006	A2	20040318	WO 2003-US328508		20030909
WO 2004022006	A3	20040715			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004018487	A1	20040129	US 2003-630590		20030729

PRIORITY APPLN. INFO.:

US 2003-630590		20030729
US 2002-409298P	P	20020909
US 2003-450464P	P	20030227
US 2003-490094P	P	20030725
US 2003-630590	A	20030729
US 2000-710059	B2	20001111
US 2001-269523P	P	20010216
US 2001-309841P	P	20010803
US 2002-80273	A2	20020219
US 2002-360061P	P	20020225

WO 2002-US24655 A2 20020802

AB The invention provides reagents and methods for detecting pathogen infections in human samples. This detection utilizes specific **proteins** to detect the presence of pathogen **proteins** or abnormal expression of human **proteins** resulting from pathogen infections. Specific methods, compns. and kits are disclosed herein for the detection of oncogenic **human papillomavirus** **E6 proteins** in clin. samples. One advantage of the invention is the use of **PDZ** domain **proteins**, which unlike **antibodies**, bind most or all oncogenic **HPV** **E6 proteins** from human papillomavirus, and, as such, make be used to diagnose cervical, and other, cancers.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 30 Jan 2004
ACCESSION NUMBER: 2004:78616 CAPLUS
DOCUMENT NUMBER: 140:144082
TITLE: Methods of diagnosis of cervical cancer by detecting oncogenic **human papillomavirus** **E6 protein** using **E6** -binding partners, such as a **PDZ** domain and an anti-E6 **antibody**
INVENTOR(S): Lu, Peter S.; Schweizer, Johannes; Diaz-Sarmiento, Chamorro Somoza; Belmares, Michael P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 168 pp., Cont.-in-part of Appl. No. PCT/US02/24655.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004018487	A1	20040129	US 2003-630590	20030729
US 2003049695	A1	20030313	US 2002-80273	20020219
WO 2003014303	A2	20030220	WO 2002-US24655	20020802
WO 2003014303	A3	20030814		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004022006	A2	20040318	WO 2003-US28508	20030909
WO 2004022006	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,				

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2004076646 A2 20040910 WO 2004-US6001 20040227
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004229298 A1 20041118 US 2004-789102 20040227

PRIORITY APPLN. INFO.:

US 2000-710059	B2	20001111
US 2001-269523P	P	20010216
US 2001-309841P	P	20010803
US 2002-80273	A2	20020219
US 2002-360061P	P	20020225
WO 2002-US24655	A2	20020802
US 2002-409298P	P	20020909
US 2003-450464P	P	20030227
US 2001-269522P	P	20010216
US 2001-269694P	P	20010216
US 2003-490094P	P	20030725
US 2003-630590	A	20030729

AB The invention provides reagents and methods for detecting pathogen infections in human samples. This detection utilizes specific **proteins** to detect the presence of pathogen **proteins** or abnormal expression of human **proteins** resulting from pathogen infections. Specific methods, compns. and kits are disclosed herein for the detection of oncogenic **human papillomavirus** **E6 proteins** in clin. samples. Suitable oncogenic E6 **protein** binding partners for E6 detection include a **PDZ** domain (particularly, from **MAGI-1**), an **antibody** against E6 **protein**; other **proteins** that recognize oncogenic E6 **protein** (e.g., p53, E6-AP or E6-BP); DNA (i.e., cruciform DNA); and other partners such as aptamers or single chain **antibodies** from phage display.

L6 1823 SEA FILE=CAPLUS ABB=ON PLU=ON (HUMAN(W)PAPILLOM? OR HPV)(5A)" E6" OR HUMAN WART VIRUS OR HPVE6
L7 26 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (PDZ? OR MAGI(2W)(I OR 1))
L8 3 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND ANTIBOD?

L9 0 L8 NOT L4

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS,

JAPIO, CANCERLIT' ENTERED AT 11:03:05 ON 03 JAN 2005)
L10 5 S L8
L11 4 DUP REM L10 (1 DUPLICATE REMOVED)

L11 ANSWER 1 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-248368 [23] WPIDS
CROSS REFERENCE: 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-122015 [12]; 2004-653410 [63]; 2004-821137 [81]
DOC. NO. CPI: C2004-097072
TITLE: Determining if a human subject is infected with an oncogenic strain of human papillomavirus (HPV) by detecting the presence of any oncogenic **HPV E6** protein bound to the **PDZ** domain polypeptide using an **HPV E6** binding partner.
DERWENT CLASS: B04 D16
INVENTOR(S): BELMARES, M P; DIAZ-SARMIENTO, C S; LU, P S; SCHWEIZER, J
PATENT ASSIGNEE(S): (ARBO-N) ARBOR VITA CORP
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004022006	A2	20040318	(200423)*	EN	234
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003270548	A1	20040329	(200459)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004022006	A2	WO 2003-US28508	20030909
AU 2003270548	A1	AU 2003-270548	20030909

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003270548	A1 Based on	WO 2004022006

PRIORITY APPLN. INFO: US 2003-630590 20030729; US 2002-409298P 20020909; US 2003-450464P 20030227; US 2003-490094P 20030725
AN 2004-248368 [23] WPIDS
CR 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-122015 [12]; 2004-653410 [63]; 2004-821137 [81]
AB WO2004022006 A UPAB: 20041216
NOVELTY - Determining if a human subject is infected with an oncogenic strain of human papillomavirus (HPV), is new.

DETAILED DESCRIPTION - Determining if a human subject is infected with an oncogenic strain of human papillomavirus (HPV) comprises:

(1) contacting a sample obtained from the subject with a **PDZ** domain polypeptide bound to a solid support; and

(2) detecting the presence of any oncogenic **HPV E6** protein bound to the **PDZ** domain polypeptide using an **HPV E6** binding partner, where the presence of oncogenic **HPV E6** protein indicates that the subject is infected with an oncogenic strain of HPV.

An INDEPENDENT CLAIM is included for a kit for testing for the presence of oncogenic **HPV E6** protein.

USE - The method is useful for determining if a human subject is infected with an oncogenic strain of HPV (claimed).

Dwg.0/11

L11 ANSWER 2 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-821137 [81] WPIDS

CROSS REFERENCE: 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-122015 [12]; 2004-248368 [23]; 2004-653410 [63]

DOC. NO. NON-CPI: N2004-648334

DOC. NO. CPI: C2004-285320

TITLE: Screening agent affecting binding of protein to **MAGI-1 PDZ** polypeptide, useful for treating cancer comprises testing candidate agent on binding of oncogenic E6 protein to protein having amino acid sequence of second **PDZ** domain from **MAGI-1**.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): BAGOWSKI, C P; BELMARES, M P; DIAZ-SARMIENTO, C S; GARMAN, J D; LU, P S; SCHWEIZER, J

PATENT ASSIGNEE(S): (BAGO-I) BAGOWSKI C P; (BELM-I) BELMARES M P; (DIAZ-I) DIAZ-SARMIENTO C S; (GARM-I) GARMAN J D; (LUPS-I) LU P S; (SCHW-I) SCHWEIZER J

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004229298	A1	20041118	(200481)*		191

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004229298	A1	CIP of	US 2000-710059	20001110
		Provisional	US 2001-269523P	20010216
		Provisional	US 2001-309841P	20010803
		CIP of	US 2002-80273	20020219
		Provisional	US 2002-360061P	20020225
		CIP of	WO 2002-US24655	20020802
		Provisional	US 2003-450464P	20030227
		Provisional	US 2003-490094P	20030725
		CIP of	US 2003-630590	20030729
			US 2004-789102	20040227

PRIORITY APPLN. INFO: US 2004-789102 20040227; US
2000-710059 20001110; US
2001-269523P 20010216; US
2001-309841P 20010803; US
2002-80273 20020219; US
2002-360061P 20020225; WO
2002-US24655 20020802; US
2003-450464P 20030227; US
2003-490094P 20030725; US
2003-630590 20030729

AN 2004-821137 [81] WPIDS
CR 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-122015 [12]; 2004-248368 [23]; 2004-653410 [63]

AB US2004229298 A UPAB: 20041216

NOVELTY - Screening (M1) agent affecting binding of oncogenic protein to **MAGI-1 PDZ** polypeptide, involves determining an effect of a candidate agent on binding of an oncogenic E6 protein to a polypeptide comprising the amino acid sequence of a second **PDZ** domain from **MAGI-1**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated peptide (I) comprising an amino acid sequence corresponding to two contiguous amino acids at the C-terminus of an oncogenic E6 protein;

(2) a pharmaceutical composition (C1) comprising (I) and a carrier; and

(3) a kit comprising (I) and instructions for using (I) to treat a cancer associated with HPV infection.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Reduces binding of **E6** protein of **human papillomavirus** (**HPV**) to **PDZ** protein such as **MAGI-1** protein (claimed).

In vitro analysis of inhibition of **PDZ** protein such as TIP1-**HPV E6** 16 binding by PL peptides was carried out as follows. The 96-well immuno-plate was coated with anti-glutathione-S-transferase (GST) **antibody** (100 micro L). The plate was tap dried after dumping excess **antibody**, blocked by adding 2% bovine serum albumin (BSA)/phosphate buffered saline (PBS) (200 micro L/well). Then, the plate was incubated for 2 hours at 4 deg. C. After rinsing with cold PBS (200 micro L/well), GST-TIP1 fusion protein (50 micro L) in 2% BSA/PBS, or GST alone as control was added to the well. The well was incubated at 4 deg. C for 1-2 hours. After rinsing excess protein, peptide mixture reagent (**HPV E6** 16+Tax peptides) (50 micro L) was added to the well, incubated on ice for 10 minutes and then at room temperature for 10 minutes. HRP-streptavidin was added, rinsed with Tween wash buffer, 3,3',5,5'-tetramethylbenzidine (TMB) substrate was added, incubated, and readings were taken at 650 nm. The result indicated a decrease in binding between TIP1 and **HPV E6** 16 by Tax PL peptide.

USE - (M1) is useful for screening agent affecting binding of oncogenic protein to **MAGI-1 PDZ** polypeptide. (I) is useful for modulating an interaction between a **MAGI-1** protein and an oncogenic E6 protein, which involves contacting the **MAGI-1** protein with (I). (I) is useful for reducing the oncogenicity of an oncogenic strain of HPV in a cell, which involves reducing binding of an **E6** protein of the **HPV**

to a **MAGI-1** protein of the cell, where the reduction of binding is done by contacting the E6 protein with (I), the cell is a cell in vitro or cell in vivo. C1 is useful for treating a cancer associated with HPV infection, which involves administering C1 to a subject who is in need of the treatment, where the subject has cervical cancer, uterine cancer, anal cancer, colorectal cancer, penile cancer, oral cancer, skin cancer or esophageal cancer (claimed).

ADVANTAGE - The agent screened by (M1) enables more specific, effective and cost-effective treatment of cancer caused by HPV infection.

DESCRIPTION OF DRAWING(S) - The figure is a graph showing the inhibition of interaction between **human papillomavirus** **E6** 16 and TIP1 by Tax peptide.

Dwg.3/11

L11 ANSWER 3 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-122015 [12] WPIDS

CROSS REFERENCE: 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-248368 [23]; 2004-653410 [63]; 2004-821137 [81]

DOC. NO. CPI: C2004-048785

TITLE: Detecting the presence of an oncogenic **human papilloma** virus (**HPV**) **E6** protein in a sample by contacting a sample suspected of containing an oncogenic **HPV E6** protein with a **PDZ** domain polypeptide.

DERWENT CLASS: B04 D16

INVENTOR(S): BELMARES, M P; DIAZ-SARMIENTO, C S; LU, P S; SCHWEIZER, J

PATENT ASSIGNEE(S): (BELM-I) BELMARES M P; (DIAZ-I) DIAZ-SARMIENTO C S; (LUPS-I) LU P S; (SCHW-I) SCHWEIZER J

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004018487	A1	20040129	(200412)*		168

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004018487	A1	CIP of	US 2000-710059	20001110
		Provisional	US 2001-269523P	20010216
		Provisional	US 2001-309841P	20010803
		CIP of	US 2002-80273	20020219
		Provisional	US 2002-360061P	20020225
		CIP of	WO 2002-US24655	20020802
		Provisional	US 2002-409298P	20020909
		Provisional	US 2003-450464P	20030227
			US 2003-630590	20030729

PRIORITY APPLN. INFO: US 2003-630590 20030729; US 2000-710059 20001110; US 2001-269523P 20010216; US 2001-309841P 20010803; US 2002-80273 20020219; US 2002-360061P 20020225; WO

2002-US24655 20020802; US
2002-409298P 20020909; US
2003-450464P 20030227

AN 2004-122015 [12] WPIDS
CR 2002-608221 [65]; 2002-674963 [72]; 2003-268193 [26]; 2004-248368 [23]; 2004-653410 [63]; 2004-821137 [81]
AB US2004018487 A UPAB: 20041216
NOVELTY - Detecting the presence of an oncogenic **human papilloma** virus (**HPV**) **E6** protein in a sample comprises:

(a) contacting a sample suspected of containing an oncogenic **HPV E6** protein with a **PDZ** domain polypeptide; and

(b) detecting any binding of the oncogenic **HPV E6** protein in the sample to the **PDZ** domain polypeptide, where binding of the oncogenic **HPV E6** protein to the **PDZ** domain polypeptide indicates the presence of an oncogenic **HPV E6** protein in the sample.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a system for detecting the presence of an oncogenic **HPV E6** polypeptide in a sample comprising a first and a second binding partner for an oncogenic **HPV E6** polypeptide, where the first binding partner is a **PDZ** domain protein and at least one of the binding partners is attached to a solid support;

(2) determining if a subject is infected with an oncogenic strain of HPV; and

(3) a kit for testing for the presence of oncogenic **HPV E6** protein, the kit comprising first and second binding partners for the oncogenic **HPV E6** protein, where the first binding partner is a **PDZ** domain protein.

USE - The method is useful for detecting the presence of an oncogenic **human papilloma** virus (**HPV**) **E6** protein in a sample (claimed).

Dwg.0/10

L11 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001029726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11077444
TITLE: Interactions of the **PDZ**-protein **MAGI-1** with adenovirus E4-ORF1 and high-risk papillomavirus E6 oncoproteins.
AUTHOR: Glaunsinger B A; Lee S S; Thomas M; Banks L; Javier R
CORPORATE SOURCE: Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX 77030, USA.
CONTRACT NUMBER: RO1CA58541 (NCI)
T32AI07471 (NIAID)
SOURCE: Oncogene, (2000 Nov 2) 19 (46) 5270-80.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

Searcher : Shears 571-272-2528

Entered Medline: 20001121

AB The oncoproteins of small DNA tumor viruses promote tumorigenesis by complexing with cellular factors intimately involved in the control of cell proliferation. The major oncogenic determinants for human adenovirus type 9 (Ad9) and high-risk human papillomaviruses (**HPV**) are the E4-ORF1 and **E6** proteins, respectively. These seemingly unrelated viral oncoproteins are similar in that their transforming activities in cells depend, in part, on a carboxyl-terminal **PDZ** domain-binding motif which mediates interactions with the cellular **PDZ**-protein DLG. Here we demonstrated that both Ad9 E4-ORF1 and high-risk **HPV E6** proteins also bind to the DLG-related **PDZ**-protein **MAGI-1**. These interactions resulted in **MAGI-1** being aberrantly sequestered in the cytoplasm by the Ad9 E4-ORF1 protein or being targeted for degradation by high-risk **HPV E6** proteins. Transformation-defective mutant viral proteins, however, were deficient for these activities. Our findings indicate that **MAGI-1** is a member of a select group of cellular **PDZ** proteins targeted by both adenovirus E4-ORF1 and high-risk **HPV E6** proteins and, in addition, suggest that the tumorigenic potentials of these viral oncoproteins depend, in part, on an ability to inhibit the function of **MAGI-1** in cells.

(FILE 'CAPLUS' ENTERED AT 11:05:21 ON 03 JAN 2005)

L12 8048 SEA FILE=CAPLUS ABB=ON PLU=ON HUMAN(W)PAPILLOM? OR HPV OR HUMAN WART VIRUS OR HPVE6

L13 26 SEA FILE=CAPLUS ABB=ON PLU=ON L12 AND (PDZ? OR MAGI(2W)(I OR 1))

L14 3 SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND ANTIBOD?

L15 0 L14 NOT L4

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 11:06:16 ON 03 JAN 2005)

L16 5 S L14

L17 0 S L16 NOT L10

(FILE 'MEDLINE' ENTERED AT 11:08:03 ON 03 JAN 2005)

L18 7464 SEA FILE=MEDLINE ABB=ON PLU=ON "PAPILLOMAVIRUS, HUMAN"/CT

L19 62452 SEA FILE=MEDLINE ABB=ON PLU=ON ANTIBODIES/CT

L20 17 SEA FILE=MEDLINE ABB=ON PLU=ON L18 AND L19

L21 123 SEA FILE=MEDLINE ABB=ON PLU=ON POLYPROTEINS/CT

L22 129774 SEA FILE=MEDLINE ABB=ON PLU=ON PROTEINS/CT

L23 79662 SEA FILE=MEDLINE ABB=ON PLU=ON PEPTIDES/CT

L24 0 SEA FILE=MEDLINE ABB=ON PLU=ON L20 AND (L21 OR L22 OR L23)

L20 ANSWER 1 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2002385747 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12133476

TITLE: Immunogenicity study of HPV 6b virus-like particles.

AUTHOR: Liu Yuehua; Liu Xiaosong; Frazer Ian H

CORPORATE SOURCE: Department of Dermatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China.

SOURCE: Zhonghua yi xue za zhi, (2002 May 10) 82 (9) 587-9.

Searcher : Shears 571-272-2528

Journal code: 7511141. ISSN: 0376-2491.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020723
Last Updated on STN: 20020910
Entered Medline: 20020909

ED Entered STN: 20020723
Last Updated on STN: 20020910
Entered Medline: 20020909

AB OBJECTIVE: To confirm human papillomavirus (HPV) 6b virus-like particles (VLP) have strong immunogenicity and the protective antibody induced by HPV 6b VLP have cross-reactive immunity against HPV11 VLP and bovine papillomavirus (BPV) 1 VLP. METHOD: The late gene L1 for HPV6b, HPV 11 and L1/L2 for BPV 1 were molecularly cloned into recombinant baculovirus, respectively. The recombinant viruses were expressed in insect cells (Sf-9 cells). The expressed L1 proteins self-assembled into virus-like particles (VLP) for HPV6b, HPV 11 and BPV 1. VLP were purified from insect cell nuclei by CsCl centrifugation. The Balb/c mice were immunized on days 0 and 21 with 50 microgramHPV6b VLP intramuscularly. Sera were collected after a further 7 days and 3 months. The titers of IgG against HPV 6b VLP, HPV 11 VLP and BPV1 VLP were detected. Hemagglutination inhibition assay was conducted to detected that whether antisera produced by HPV 6b VLP immunization could inhibit HPV11 VLP and BPV 1 VLP agglutinate mouse red blood cells. RESULT: After 7 days of two immunizations, the titers of IgG against HPV6b VLP, HPV11 VLP and BPV1 VLP were 1:6 400, 1:1 600 and 1:1 600 by ELISA, respectively. Three months later, the titers of IgG against HPV6b VLP, HPV11VLP and BPV1 VLP were 1:800, 1:400 and 1:100, respectively. Hemagglutination inhibition assay results showed that the antisera produced by HPV6b VLP inhibit HPV6b VLP and HPV11 VLP to mouse red blood cells binding. CONCLUSION: HPV 6b VLP have potent immunogenicity. Antisera produced by HPV6b VLP could inhibit the binding of HPV6b VLP and HPV11 VLP and cells. Both HPV6b and HPV11 share neutralizing epitopes which are cross-reactive and HPV6b VLP may be used in prophylactic and therapeutic vaccine for HPV6b and/or HPV 11 infections.

L20 ANSWER 2 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002247926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11986752
TITLE: Establishment of a sandwich ELISA method for detection of reporter chloramphenicol acetyltransferase gene.
AUTHOR: Gao Chen; Hou Xingsheng; Zhang Fuping; Zhou Wei; Yuan Yukang; Dong Xiaoping
CORPORATE SOURCE: Institute of Virology, Chinese Academy of Preventive Medicine, Beijing 100052, China.
SOURCE: Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he linchuang bingduxue zazhi = Chinese journal of experimental and clinical virology, (2002 Mar) 16 (1) 69-73.
Journal code: 9602873. ISSN: 1003-9279.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese

Searcher : Shears 571-272-2528

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020503
Last Updated on STN: 20030204
Entered Medline: 20030203

ED Entered STN: 20020503
Last Updated on STN: 20030204
Entered Medline: 20030203

AB BACKGROUND: To establish a sandwich ELISA method for detection of reporter chloramphenicol acetyltransferase (CAT) gene. METHODS: The full length sequence of CAT gene was amplified with PCR using plasmid pBLCAT6 as template, and inserted into the prokaryotic expression plasmid Pgex-2T. The purified fusion protein was emulsified with complete or incomplete Freund adjuvant and injected subcutaneously into rabbits. The antibody was labeled with biotin, and a sandwich ELISA technique with biotin streptavidin amplify system was established. Several CAT reporter plasmids containing different HPV 16 LCR sequences were generated and transfected transiently to monolayer cells in vitro. The cytoplasm proteins were extracted and the expressions of CAT were evaluated with the newly established ELISA assay. RESULTS: SDS-PAGE displayed that the molecular weight of the expressed fusion protein was about 54,000. The prepared antiserum was able to recognize the CAT protein expressed by mammalian cells or prokaryote cells. Under the control of different promoters and their regulate sequences,two to eight folds CAT expression increased were evaluated in transiently transfected mammalian cells by the newly established sandwich ELISA method. CONCLUSIONS: The established method could sensitively reflect the activities of the upstream promoters, as well as the influence of exchanges of nucleotides within the regulate region on the promoter activities. Therefore, it proposes a convenient assay for the studies using CAT as the reporter gene.

L20 ANSWER 3 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2001639755 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11641258
TITLE: Dendritic cells induce the death of human papillomavirus-transformed keratinocytes.
AUTHOR: Hubert P; Giannini S L; Vanderplasschen A; Franzen-Detrooz E; Jacobs N; Boniver J; Delvenne P
CORPORATE SOURCE: Department of Pathology, University Hospital of Liege, CHU Sart Tilman, 4000 Liege, Belgium.. P.Hubert@ulg.ac.be
SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2001 Nov) 15 (13) 2521-3.
Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20030105
Entered Medline: 20011205

ED Entered STN: 20011107
Last Updated on STN: 20030105
Entered Medline: 20011205

AB Although human papillomavirus (HPV) antigens are expressed in a majority

of (pre)neoplastic lesions (squamous intraepithelial lesions; SILs) of the uterine cervix, progression to invasive cancer may occur, which suggests that the presentation of viral antigens to the immune system is deficient in some SILs. To determine whether professional antigen-presenting cells die in SILs, we assayed for the apoptosis of immature dendritic cells (DC) in organotypic cultures of HPV-transformed keratinocytes, which reproduce many features of in vivo observed SILs. Unexpectedly, the infiltration of organotypic cultures by DC specifically induced the apoptosis of HPV+ tumor cells, whereas DC were not affected. In the same conditions and in coculture experiments, apoptosis was not observed in normal keratinocytes. The induction of apoptosis required membrane contacts between DC and HPV-transformed keratinocytes. Although the HPV+cell lines were sensitive to the effects of TRAIL, soluble TRAILR2-Fc did not block the DC-induced apoptosis. Furthermore, although FasL and Fas were detected on DC and HPV+ cell lines, respectively, functional analysis revealed that this pathway is not responsible for the apoptosis induced by the DC. All together these results suggest that DC may be at the interface between innate and adaptive immunity by inducing the apoptosis of (pre)neoplastic cells.

L20 ANSWER 4 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2000254543 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10795526
TITLE: High prevalence of serum antibodies to Ras and type 16 E4 proteins of human papillomavirus in patients with precancerous lesions of the uterine cervix.
AUTHOR: Pedroza-Saavedra A; Cruz A; Esquivel F; De La Torre F; Berumen J; Gariglio P; Gutierrez L
CORPORATE SOURCE: Centro de Investigaciones Sobre Enfermedades Infecciosas, Instituto Nacional de Salud Publica, Cuernavaca, Morelos, Mexico.
SOURCE: Archives of virology, (2000) 145 (3) 603-23.
Journal code: 7506870. ISSN: 0304-8608.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000515

ED Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000515

AB Serum samples from 38 healthy women and 55 women with different types of cervical lesions were investigated for the presence of antibodies to Ras and against E4 and E7 proteins of human papillomavirus type 16 (HPV-16). Our results showed that anti-E7 antibodies were closely associated with cervical cancer (75%), as previously reported. Interestingly, E4 antibodies showed higher prevalence in condyloma lesions (79%; 11/14) than in cervical cancer (60%; 12/20). We also identified 11% (4/38) of healthy individuals as positive for E4 antibodies, which suggests an early immune recognition of this protein. Patients with condyloma and cervical intraepithelial neoplasia (CIN) also showed higher prevalences of Ras antibodies (approximately 40%) than cervical cancer patients (10%; 2/20). By sequencing part of the ras genes and using different Ras antigens, we

showed that serum antibodies from patients were not directed to a Ras mutation, since wild-type cHa-Ras protein was recognized by these antibodies. In addition, patients positive for Ras antibodies (94%) were also positive for E4 antibodies, suggesting an association between these. The high prevalence of antibodies against Ras and E4 proteins in pre-malignant lesions opens the possibility of using both antibodies as early markers for potential cervical cancer patients.

L20 ANSWER 5 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1999443703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10515680
TITLE: Molecular analysis of resistance to interferon in patients with laryngeal papillomatosis.
AUTHOR: Garcia-Millian R; Santos A; Perea S E; Gonzalez-Cabanas R; Valenzuela C; Arana M
CORPORATE SOURCE: Department of Cellular Biology, Center for Biological Research, Havana, Cuba.. farma3@cigb.edu.cu
SOURCE: Cytokines, cellular & molecular therapy, (1999 Jun) 5 (2) 79-85.
Journal code: 9713367. ISSN: 1368-4736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991122
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991122
AB Although interferon (IFN)-alpha has been used successfully as an adjuvant therapy in laryngeal papillomatosis, some patients are resistant to this treatment. In order to know which patients will benefit from the therapy, we have tried to find a relationship between the IFN response and the viral and host parameters in the lesion. Detection of viral type and copy numbers by polymerase chain reaction (PCR) showed that all patients infected with human papillomavirus (HPV)-11 were sensitive to the treatment, in contrast to those infected with HPV-6. These differences could be explained in part by the inability of HPV-11 E7 to inhibit the induction of an IFN-responsive element, whereas HPV-6 E7 almost completely inhibited the activity of this promoter in transient transfection experiments. Local immune status in the lesion showed that all HPV-11-infected patients had detectable levels of interleukin (IL)-15 and IFN-gamma mRNA, in contrast to HPV-6-infected patients, in whom mRNA for these cytokines was almost absent. Viral copy numbers and levels of IL-4 mRNA could not be correlated with IFN response. Only one patient resistant to recombinant IFN-alpha2b and negative for HPV DNA presented high titers of neutralizing anti-IFN-alpha2b antibodies. This patient became sensitive when natural IFN-alpha was administered. These results suggest that response to IFN may be a complex phenomenon resulting from the interaction between viral and host elements.

L20 ANSWER 6 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1999348116 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10417539

TITLE: Does plantar epidermoid cyst with human papillomavirus infection originate from the eccrine dermal duct?.
AUTHOR: Abe H; Ohnishi T; Watanabe S
SOURCE: British journal of dermatology, (1999 Jul) 141 (1) 161-2. Journal code: 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302
ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302

L20 ANSWER 7 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1999180764 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10079255
TITLE: Colonization of in vitro-formed cervical human papillomavirus- associated (pre)neoplastic lesions with dendritic cells: role of granulocyte/macrophage colony-stimulating factor.
AUTHOR: Hubert P; van den Brule F; Giannini S L; Franzen-Detrooz E; Boniver J; Delvenne P
CORPORATE SOURCE: Department of Pathology, University Hospital of Liege, Liege, Belgium.. p.hubert@ulg.ac.be
SOURCE: American journal of pathology, (1999 Mar) 154 (3) 775-84. Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
ED Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
AB The purpose of this study was to investigate the ability of CD1a+ Langerhans/dendritic cells (LCs/DCs) to infiltrate human papillomavirus (HPV)-associated (pre)neoplastic lesions of the uterine cervix. Migration of LCs/DCs in the presence of keratinocytes derived from normal cervix and HPV-transformed cell lines was evaluated in Boyden chambers and in organotypic cultures and correlated with granulocyte/macrophage colony-stimulating factor (GM-CSF) production by the cells, as determined by ELISA. Conditioned media of HPV-transformed keratinocytes contained lower amounts of GM-CSF and induced a decreased motile response of LCs/DCs in the Boyden chamber assay compared with those of normal cervical keratinocytes. The migration of LCs/DCs in the presence of conditioned media from normal keratinocytes could be blocked by an anti-GM-CSF antibody, and the migration of LCs/DCs in the presence of conditioned media from HPV-transformed keratinocytes could be increased by supplementing the media with recombinant GM-CSF. GM-CSF was also a potent

factor in enhancing the colonization of LCs/DCs into organotypic cultures of HPV-transformed keratinocytes, as the infiltration of LCs/DCs in the in vitro-formed (pre)neoplastic epithelium was minimal under basal conditions and dramatically increased after the addition of GM-CSF to the cultures. These results suggest that GM-CSF could play an important role in the recruitment of LCs/DCs into the HPV-transformed (pre)neoplastic cervical epithelium and be useful as a new immunotherapeutic approach for cervical (pre)cancers.

L20 ANSWER 8 OF 17 MEDLINE on STN
ACCESSION NUMBER: 1999069426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9852095
TITLE: E3-ubiquitin ligase/E6-AP links multicopy maintenance protein 7 to the ubiquitination pathway by a novel motif, the L2G box.
AUTHOR: Kuhne C; Banks L
CORPORATE SOURCE: International Centre for Genetic Engineering and Biotechnology, Padriciano 99, I-34012 Trieste, Italy.. kuehne@icgeb.trieste.it
SOURCE: Journal of biological chemistry, (1998 Dec 18) 273 (51) 34302-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990209
Last Updated on STN: 20030304
Entered Medline: 19990126
ED Entered STN: 19990209
Last Updated on STN: 20030304
Entered Medline: 19990126
AB Ubiquitin ligases are generally assumed to play a major role in substrate recognition and thus provide specificity to a particular ubiquitin modification system. The multicopy maintenance protein (Mcm) 7 subunit of the replication licensing factor-M was identified as a substrate of the E3-ubiquitin ligase/E6-AP by its interaction with human papillomavirus-18E6. Mcm7 is ubiquitinated in vivo in both an E6-AP-dependent and -independent manner. E6-AP functions in these reactions independently of the viral oncogene E6. We show that recognition of Mcm7 by E6-AP is mediated by a homotypic interaction motif present in both proteins, called the L2G box. These findings served as the basis for the definition of substrate specificity for E6-AP. A small cluster of proteins whose function is intimately associated with the control of cell growth and/or proliferation contains the L2G box and is thereby implicated in an E6-AP and, by default, HPV-E6-dependent ubiquitination pathway.

L20 ANSWER 9 OF 17 MEDLINE on STN
ACCESSION NUMBER: 97433113 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9288782
TITLE: Inhibitors of epidermal growth factor receptor kinase and of cyclin-dependent kinase 2 activation induce growth arrest, differentiation, and apoptosis of human papilloma virus 16-immortalized human keratinocytes.

AUTHOR: Ben-Bassat H; Rosenbaum-Mitrani S; Hartzstark Z; Shlomai Z; Kleinberger-Doron N; Gazit A; Plowman G; Levitzki R; Tsvieli R; Levitzki A
CORPORATE SOURCE: Laboratory of Experimental Surgery, Hadassah University Hospital, Jerusalem, Israel.
SOURCE: Cancer research, (1997 Sep 1) 57 (17) 3741-50.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970924

ED Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970924

AB Human papilloma virus 16 (HPV 16) is associated with cervical cancer and is therefore considered a major health risk for women. Immortalization of keratinocytes induced by HPV infection is largely due to the binding of p53 and Rb by the the viral oncoproteins E6 and E7, respectively, and is driven to a large extent by a transforming growth factor alpha/amphiregulin epidermal growth factor receptor autocrine loop. In this study, we show that the growth of HPV 16-immortalized human keratinocytes can be blocked by a selective epidermal growth factor receptor kinase inhibitor, AG 1478, and by AG 555, a blocker of cyclin-dependent kinase 2 (Cdk2) activation. AG 1478 induces a massive increase in the Cdk2 protein inhibitors p27 and p21, whereas AG 555 appears to have a different mechanism of action, inhibiting the activation of Cdk2. Growth arrest induced by AG 1478 and AG 555 is accompanied by up to 20% of cells undergoing apoptosis. Following AG 1478 treatment but not AG 555 treatment, up to 50% of cells undergo terminal keratinocyte differentiation as determined by filaggrin expression and by the decline in the expression of cytokeratin 14. The growth-arresting properties of AG 1478 and AG 555 identifies them as possible lead antipapilloma agents.

L20 ANSWER 10 OF 17 MEDLINE on STN
ACCESSION NUMBER: 97201085 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9038265
TITLE: Antibody levels against alpha-galactosyl epitopes in sera of patients with squamous intraepithelial lesions and early invasive cervical carcinoma.
AUTHOR: Tremont-Lukats I W; Avila J L; Hernandez D; Vasquez J; Teixeira G M; Rojas M
CORPORATE SOURCE: Instituto Oncologico Luis Razetti, Universidad Central de Venezuela, Caracas, Venezuela.
SOURCE: Gynecologic oncology, (1997 Feb) 64 (2) 207-12.
Journal code: 0365304. ISSN: 0090-8258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19970407

Searcher : Shears 571-272-2528

Entered Medline: 19970327

ED Entered STN: 19970407
Last Updated on STN: 19970407
Entered Medline: 19970327

AB We measured serum levels of anti-Gal(alpha 1-->3)Gal and anti-Gal(alpha 1-->2)Gal antibodies in 89 and 91 women, respectively, by using ELISA. These patients had cervical intraepithelial neoplasia (CIN) grades 1 to 3 and early invasive cervical carcinoma (ICC). Our objective was to compare anti-alpha-galactosyl antibody levels among them and with those of normal controls. High levels of anti-Gal(alpha 1-->2)Gal antibodies were detected in 22% of patients (P = 0.006). The mean level was 1.6 times greater than that of controls, without difference among subgroups. Thirty percent of patients had abnormally high anti-Gal levels (P = 0.001). Mean levels were twofold greater than the mean control value. Subsets with human papillomavirus/CIN 1 and CIN 2-3 had high immunoreactivity (P = 0.004). Both antibodies showed a significant correlation (r = 0.53, P < 0.00001). We conclude that 22 to 30% of patients with CIN 1-3 showed significantly high levels of anti-alpha-galactosyl antibodies. This seroreactivity might be related to the abnormal expression of alpha-galactosyl residues at some point of the natural history of human papillomavirus infection of the uterine cervix, suggesting an active immune response by natural antibodies against this virus. Further studies are needed to determine whether anti-alpha-galactosyl antibodies confer protection in human papillomavirus infection.

L20 ANSWER 11 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95395304 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7665926
TITLE: Titration of HPV-11 infectivity and antibody neutralization can be measured in vitro.
AUTHOR: Smith L H; Foster C; Hitchcock M E; Leiserowitz G S; Hall K; Isseroff R; Christensen N D; Kreider J W
CORPORATE SOURCE: Department of Obstetrics and Gynecology, UC Davis School of Medicine 95816, USA.
SOURCE: Journal of investigative dermatology, (1995 Sep) 105 (3) 438-44.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 19951020
Entered Medline: 19951012

ED Entered STN: 19951020
Last Updated on STN: 19951020
Entered Medline: 19951012

AB Human papillomavirus type 11 (HPV-11), produced from the athymic mouse xenograft system, was shown to infect cultured neonatal human foreskin keratinocytes and the HaCaT keratinocyte cell line in vitro. Infection was documented by the appearance of HPV-11-specific spliced mRNA, detected by reverse transcriptase-polymerase chain reaction. Purified HPV-11 virions at concentrations of approximately 10(7) particles/ml could successfully evoke infection in this system. Infection was completely abrogated by preincubation of the HPV-11 inoculum with mouse anti-HPV-11

monoclonal antibodies, experimentally immunized animal sera, or sera of human patients with HPV infection. Concurrent detection of cellular mRNA for the beta-actin gene, also by reverse transcriptase-polymerase chain reaction, provided an internal control confirming RNA recovery and successful reverse transcriptase-polymerase chain reaction. Using this approach, it was possible to determine semiquantitative titers for test solutions of HPV-11-neutralizing antibodies. The in vitro system for HPV-11 infectivity and neutralization may be useful in the study of the immune response to HPV-11 infection or immunization in patients.

L20 ANSWER 12 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95373140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7645215
TITLE: The HPV16 E5 protein: expression, detection, and stable complex formation with transmembrane proteins in COS cells.
AUTHOR: Hwang E S; Nottoli T; Dimaio D
CORPORATE SOURCE: Department of Genetics, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
CONTRACT NUMBER: CA09159 (NCI)
CA16038 (NCI)
CA37157 (NCI)
SOURCE: Virology, (1995 Aug 1) 211 (1) 227-33.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950918
ED Entered STN: 19950930
Last Updated on STN: 19950930
Entered Medline: 19950918
AB The human papillomavirus-16 (HPV16) E5 gene is able to induce stable growth transformation and transient mitogenic stimulation in a variety of cultured cell systems. To characterize the biochemical properties of the hydrophobic HPV16 E5 transforming protein, we have constructed vectors expressing the wild-type HPV16 E5 gene and have generated antipeptide antisera. The 10-kDa E5 protein was readily detectable in transfected COS monkey cells by using these antisera either for immunoprecipitation of metabolically labeled cells or for immunoblotting. Coimmunoprecipitation analysis of cells coexpressing the viral protein and various growth factor receptors demonstrated stable complex formation between the E5 protein and the epidermal growth factor receptor, platelet-derived growth factor beta receptor, colony stimulating factor-1 receptor, and p185neu. The E5 protein also formed a stable complex with the vesicular stomatitis virus glycoprotein. These experiments indicated that the HPV16 E5 protein was able to participate in complex formation with a variety of transmembrane proteins, a property which may contribute to the biological activities of the viral protein. In addition, the expression vectors and antibodies described here will be useful reagents in examining various aspects of HPV16 E5 expression and function.

L20 ANSWER 13 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95251779 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7537506
TITLE: The expressed L1 proteins of HPV-1, HPV-6, and HPV-11 display type-specific epitopes with native conformation and reactivity with neutralizing and nonneutralizing antibodies.
AUTHOR: Hines J F; Ghim S J; Christensen N D; Kreider J W; Barnes W A; Schlegel R; Jenson A B
CORPORATE SOURCE: Department of Pathology, Georgetown University Medical Center, Washington, DC 20007-2197, USA.
CONTRACT NUMBER: R01CA47622 (NCI)
R01CA50812 (NCI)
R01CA57994 (NCI)
SOURCE: Pathobiology : journal of immunopathology, molecular and cellular biology, (1994) 62 (4) 165-71.
Journal code: 9007504. ISSN: 1015-2008.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
Last Updated on STN: 19990129
Entered Medline: 19950606
ED Entered STN: 19950615
Last Updated on STN: 19990129
Entered Medline: 19950606
AB Previous studies demonstrated that the human papillomavirus (HPV) type 1 L1 protein, expressed in cos cells by an SV40-based vector, displays conformational epitopes characteristic of native virions. In this study, we analyzed the expression of HPV-1, HPV-6, and HPV-11 L1 proteins in order to determine the forms of conformational epitopes expressed by recombinant L1 proteins. Using both immunofluorescence and immunoprecipitation techniques, polyclonal and monoclonal antibodies (MAbs) generated against native HPV-11 virions reacted with expressed L1 proteins of HPV-6 and/or HPV-11, but not HPV-1. Similarly, polyclonal antibodies and MAbs generated against HPV-1 virions reacted with the expressed L1 protein of HPV-1, but not HPV-6 or HPV-11. Of two MAbs that neutralized HPV-11 infection of murine fetal foreskin xenografts, one reacted with the expressed L1 protein of both HPV-6 and HPV-11, and the other reacted with HPV-11 only. A nonneutralizing conformationally dependent MAb reacted with the expressed L1 protein of both HPV-6 and HPV-11. These results demonstrate that expressed HPV L1 proteins retain type-specific, neutralizing, and nonneutralizing conformational epitopes and that cos cells may be utilized to evaluate host immune responses to such epitopes.

L20 ANSWER 14 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95047752 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7525426
TITLE: Role of conformational epitopes expressed by human papillomavirus major capsid proteins in the serologic detection of infection and prophylactic vaccination.
COMMENT: Comment in: Gynecol Oncol. 1994 Oct;55(1):10-2. PubMed ID: 7525423
AUTHOR: Hines J F; Ghim S J; Christensen N D; Kreider J W; Barnes W A; Schlegel R; Jenson A B

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Department of Obstetrics and Gynecology, Georgetown University Medical Center, Washington, DC 20007.
CONTRACT NUMBER: R01CA50812 (NCI)
R01CA57994 (NCI)
R01CA47622 (NCI)
SOURCE: Gynecologic oncology, (1994 Oct) 55 (1) 13-20.
Journal code: 0365304. ISSN: 0090-8258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 20021217
Entered Medline: 19941128
ED Entered STN: 19950110
Last Updated on STN: 20021217
Entered Medline: 19941128
AB Human papillomaviruses (HPVs) cause a variety of cutaneous warts, mucosal condylomata, and dysplasias and are etiologic in cervical cancer. Papillomavirus (PV) conformational epitopes on the surface of virions are type-specific and are the target of neutralizing antibodies. In this study, we describe two methods of in vitro expression of HPV major capsid (L1) proteins which mimicked conformational epitopes and demonstrate their type specificity and ability to react with neutralizing and/or conformation-dependent antibodies. The L1 open reading frames (ORFs) for HPV-1, 6, 11, and 16 were molecularly cloned into a SV 40 expression vector and the encoded gene products were expressed in mammalian (cos) cells. Similarly, the L1 ORFs for HPV-6, 11, 16, and 18 were molecularly cloned into recombinant baculovirus and the encoded gene products were expressed in insect (SF9) cells. The expressed L1 proteins reacted by immunofluorescence and immunoprecipitation with polyclonal and monoclonal antibodies generated against their corresponding native virions and by Western blotting with antibodies that recognized nonconformational epitopes of denatured virions. The recombinant L1 proteins expressed conformational epitopes in both cos and Sf9 cells that were type-specific and displayed neutralizing epitopes. The ability to express, purify, and qualitate the reactivity of recombinant L1 proteins will now permit the serologic analysis of host response to HPV infection and the development of prophylactic PV subunit vaccines.

L20 ANSWER 15 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95039723 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7952022
TITLE: Procedure for refolding and purification of recombinant proteins from Escherichia coli inclusion bodies using a strong anion exchanger.
AUTHOR: Suttnar J; Dyr J E; Hamsikova E; Novak J; Vonka V
CORPORATE SOURCE: Department of Biochemistry, Institute of Hematology and Blood Transfusion, Prague, Czech Republic.
SOURCE: Journal of chromatography. B, Biomedical applications, (1994 Jun 3) 656 (1) 123-6.
Journal code: 9421796. ISSN: 0378-4347.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941130

ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941130

AB Using Escherichia coli system expressing papilloma virus HPV16 E7MS2 fusion protein as a model system, a novel procedure was applied to solubilize, purify and refold recombinant proteins from E. coli inclusion bodies. The necessity to reactivate proteins at low protein concentrations (owing to their tendency to aggregate at high concentrations) was overcome by solubilization of inclusion bodies in alkaline solution and immobilization of proteins on a strong and resistant anion exchanger. This procedure has an inherent advantage of combining refolding and purification procedures in one step. The solubilization of the fusion protein in an alkaline reagent with the use of an anion exchanger resulted in considerable purification of the recombinant protein at a fairly high concentration. The protein was soluble under mild conditions and reacted with antibodies against the "native" papilloma virus.

L20 ANSWER 16 OF 17 MEDLINE on STN
ACCESSION NUMBER: 95014136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7523366
TITLE: Cell-free replication of the human papillomavirus DNA with homologous viral E1 and E2 proteins and human cell extracts.
AUTHOR: Kuo S R; Liu J S; Broker T R; Chow L T
CORPORATE SOURCE: Department of Biochemistry, University of Rochester School of Medicine and Dentistry, New York 14642.
CONTRACT NUMBER: CA36200 (NCI)
SOURCE: Journal of biological chemistry, (1994 Sep 30) 269 (39) 24058-65.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19990129
Entered Medline: 19941027

ED Entered STN: 19941222
Last Updated on STN: 19990129
Entered Medline: 19941027

AB We have established the first homologous cell-free DNA replication system for a papillomavirus. The replication of the human papillomavirus type 11 (HPV-11) origin was achieved by using human 293 cell extracts supplemented with the HPV-11 E1 and E2 proteins purified from insect cells infected with recombinant baculoviruses. Efficient replication depends on the HPV-11 origin, the HPV-11 E1 and E2 proteins, as well as human DNA polymerase alpha, delta, replication protein A, topoisomerase I, and topoisomerase II. High concentrations of E1 protein also promoted a low level of origin-independent replication which was suppressed by the

addition of the E2 protein, whereas E2 protein stimulated origin-dependent replication. We also show that an intact E2 protein binding site was absolutely necessary for origin activity, as a strong HPV-11 origin was rendered inactive when one half-site of each of the three E2 binding sites was mutated. In contrast, there was only a relatively small reduction in this mutant origin activity when the cell extracts were supplemented with the bovine papillomavirus type 1 (BPV-1) proteins. These results suggest that the HPV-11 E2 protein plays a primary role in HPV origin recognition. Furthermore, unlike transient replication in which HPV-11 and BPV-1 viral proteins promote efficient replication of homologous and heterologous origins, efficient cell-free replication took place only with the homologous combinations.

L20 ANSWER 17 OF 17 MEDLINE on STN
ACCESSION NUMBER: 94265160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7515765
TITLE: Epidermal growth factor suppresses insulin-like growth factor binding protein 3 levels in human papillomavirus type 16-immortalized cervical epithelial cells and thereby potentiates the effects of insulin-like growth factor 1.
AUTHOR: Hembree J R; Agarwal C; Eckert R L
CORPORATE SOURCE: Department of Physiology and Biophysics, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4970.
CONTRACT NUMBER: AR49750 (NIAMS)
DK07319 (NIDDK)
SOURCE: Cancer research, (1994 Jun 15) 54 (12) 3160-6.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940721
Last Updated on STN: 20000303
Entered Medline: 19940713
ED Entered STN: 19940721
Last Updated on STN: 20000303
Entered Medline: 19940713
AB Human ectocervical epithelial cells are a primary target for infection by oncogenic papillomaviruses, which are strongly implicated as causative agents in the genesis of cervical cancer. Growth factors have been implicated as agents that stimulate proliferation and enhance the possibility of malignant transformation. In the present study we utilize several human papillomavirus (HPV) type 16-immortalized ectocervical epithelial cell lines to investigate the effects of epidermal growth factor (EGF) and insulin-like growth factor I (IGF-I) on cell proliferation and the production of IGF binding proteins (IGFBPs). ECE16-1 cells, an HPV16-immortalized/nontumorigenic cell line, maintained in defined medium, produce and release high levels of IGFBP-3 (38/42 kDa) as well as smaller amounts of a 24-kDa IGFBP. Supplementation of defined medium with EGF causes a dose-dependent increase in cell growth and a concomitant decrease in the levels of IGFBP-3 released into the culture medium. EGF suppression of IGFBP-3 is maintained even when EGF-stimulated cell growth is suppressed 67% due to the simultaneous presence of 3 ng/ml of TGF beta 1, indicating that EGF suppression of IGFBP-3 levels is

independent of EGF effects on cell growth. EGF suppression of IGFBP-3 production is correlated with a reduction in IGFBP-3 mRNA level. In the presence of EGF, the growth response of the cells to ng amounts of IGF-I is significantly enhanced. Moreover, the simultaneous presence of both EGF and IGF-I reduces the level of IGFBP-3 more efficiently than EGF alone. We also observe that the IGFBP-3 level is decreased and the 24-kDa IGFBP level is increased in HPV16-positive tumorigenic versus nontumorigenic cell lines. This is the first report of EGF acting as a positive regulator of IGF-I action via the IGFBPs. On the basis of these findings, we propose that EGF stimulates ECE16-1 cell growth via a dual-action mechanism by (a) stimulating growth directly via the EGF mitogenic pathway and (b) stimulating growth indirectly by reducing the levels of inhibitory IGFBPs and thereby potentiating the effects of IGF-I. In addition, the observation that more highly transformed cell types produce lower levels of IGFBP-3 and higher levels of 24-kDa IGFBP suggests that tumor cells in more advanced cervical cancers may have an altered response to IGF-I.

FILE 'HOME' ENTERED AT 11:10:00 ON 03 JAN 2005